

REMARKS

Favorable consideration and allowance by the Examiner of the claims presented herein, i.e., Claims 1-7, 9-21, 23-43, 45-61, 63-80 and 82-144, are respectfully requested in light of the remarks which follow.

This preliminary amendment is being submitted together with (1) an Information Disclosure Statement and PTO Form 1449, (2) a Request for Continued Examination and (3) a Declaration of Todd M. Boyce and Albert Manrique Under 37 C.F.R. §1.131.

Applicants have added new Claims 135-144 herein which are similar to the previously finally rejected claims but differ therefrom in additionally reciting the term "covalent" as defining the type of chemical linkage that exists between the surface-exposed collagen of adjacent bone-derived elements in the claimed osteoimplant. Support for the term "covalent" is found in the specification at page 14, lines 13-18.¹ Although the term "covalent" does not explicitly appear therein, the specification implicitly, i.e., inherently, describes covalent bonding in that functional reactive groups on the chemical crosslinking agent react with functional groups on the exposed collagen molecules of adjacent bone-derived elements to form a reinforcing cross-bridge bonding such elements to each other.

¹ The cited text in the specification reads as follows:

Chemical crosslinking agents include those that contain bifunctional or multifunctional reactive groups, and which react with functional groups on amino acids such as epsilon-amine functional group of lysine or hydroxy-lysine, or the carboxyl functional groups of aspartic and glutamic acids. By reacting with multiple functional groups on the same or different collagen molecules, the reacting chemical crosslinking agent forms a reinforcing cross-bridge.

In the previous Office Action, the Examiner has finally rejected 1-7, 9-11, 13, 14, 19-21, 23, 24, 34-43, 45, 56-61, 63, 74-80, 82 and 93-94 under 35 U.S.C. §102(b) as anticipated by Lyle U.S. Patent No. 5,061,286 ("Lyle").

The Examiner's attention is again drawn to the publications cited and the arguments made in applicants' Amendment filed January 23, 2003.² The Examiner has not adequately addressed the content and thrust of these literature references, namely, that cyanoacrylate monomer cures by anionic polymerization, which is to say, its ethylenic unsaturation is consumed by an addition reaction, not by a reaction with reactive groups in or on surface-exposed collagen. Cyanoacrylate adhesives do not form chemical bonds with the surface to which they are applied but form polymer bonds within the adhesive itself as a result of a polymerization reaction.

The Examiner issued a final Office Action on April 2, 2003 in which he stated that he was not convinced of the fact that the chemical linkages of Lyle are produced within the adhesive and not within the collagen of the demineralized bone. The Examiner has provided no facts in support of his position. Indeed, the Examiner's position is believed to be unsupportable in view of the aforementioned publications as well as the two additional publications annexed hereto.

The Internet publication "The Chemistry and Physics of Non-Stick Coatings" (<http://www.kiss-cote.com/science/chemtxt.htm>) (printout attached) at page 3 describes

² Courtney et al., "Advances in Cyanoacrylate Technology for Device Assembly", Medical Device & Diagnostic Industry, September, 1999, available on the Internet at <http://www.devicelink.com/mddi/archive/99/09/006.html>; and Schwade, N.D., "Wound Adhesives, 2-Octyl Cyanoacrylate" eMedicine, April 10, 2002, available on the Internet at <http://www.emedicine.com/ent/topic375.htm>.

how ordinary adhesives make things stick together. Although cyanoacrylate adhesives aren't mentioned by name, the article clearly has these and similar polymeric adhesives in mind when it says:

Mechanisms of adhesion are all also governed by similar principles - whether you are referring to dental plaque sticking to teeth, barnacles sticking to boat hulls, fiberglass parts sticking in a mold or graffiti painted on a wall. The significant differences are the specific agents involved and the magnitudes involved - what kinds of materials are sticking together with what glue and the size of the parts that are sticking together.

Chemical adhesion is when two adjacent materials chemically interact with each other. This may be compared to letters in one word interacting with or being used as parts of another adjacent word, such as words in a cross-word puzzle or the game of Scrabble. Some letters are used frequently to make words while other letters do not fit easily into words, like the many words using the letter "s" and the few words with the letter "z". Some of the chemical elements and molecules interact readily with other elements, some elements and molecules do not react readily.

True chemical adhesion does not occur often. In fact, most glues that are available today do not chemically bond with a surface.

Most adhesives act as luting agents, covering the opposing surfaces and making them "fit" together intimately. The more intimate the fit, the better the mechanical retention. Consider a rubber pad on a wet counter top. The water is providing the intimate fit, "wetting" both surfaces. Because of the hydrostatic seal that forms, it is nearly impossible to lift the pad off the counter.



Glues also make things stick together by "locking" into mechanical undercuts on the surfaces of the parts, filling in and hardening in the pits and valleys in the finish of the surface. This mechanical retention is simply one material getting physically "hooked on to" another material.

According to the foregoing explanation, the nature of the adhesion for most adhesives, and this would include cyanoacrylate adhesives as the next publication makes clear, is one of mechanical retention, not chemical bond formation. The other publication (printout attached) is a posting on an internet bulletin board www.madsci.org/posts/archives/apr2000/955665848.Ch.r.html also explaining how glues/adhesives work. According to this posting (emphasis added):

Other types of adhesives (epoxies and *cyanoacrylates*, for example) form the polymer in situ; this gives them greater penetrating power, because the small molecules can penetrate smaller pores before they link up into the polymer network.

But in no case do you ever get a chemical bond between glue and substrate.

This is essentially a description of the mechanical retention mechanism of adhesion described in the internet publication "The Chemistry and Physics of Non-Stick Coatings" discussed above and is specifically applicable to epoxies and *cyanoacrylates*.

It is respectfully submitted that the foregoing publications, including those already of record, provide compelling evidence in support of the conclusion that cyanoacrylate adhesives as disclosed in Lyle work in a mechanical fashion and not by covalent bonding as in the amended claims herein.

Based on the foregoing, applicants submit that Claims 1-7, 9-21, 23-43, 45-61, 63-80 and 82-144 are patentable over Lyle.

In the final Office Action of April 2, 2003, the Examiner rejected Claims 1-7, 9-21, 23-43, 45-61 and 82-134 under 35 U.S.C. § 102(e) as anticipated by the Boyce et al. '939 patent. In an effort to antedate this patent, applicants responded to this rejection by submitting a declaration under Rule 131. In the Advisory Action of May 28, 2003, the Examiner stated that the declaration is insufficient to show that applicants had completed the invention, that it worked for its intended purpose and that it had the claimed properties such as compression strength.

Applicants submit herewith a Declaration of Todd M. Boyce and Albert Manrique under 37 C.F.R. § 1.131 with Exhibits A, B and C annexed thereto. As detailed in this declaration, the marked-up draft patent application constituting part of Exhibit A evidences the conception of the subject matter of Claim 1 herein and the subject matter of the other rejected claims. The declaration further evidences diligence from just prior to the January 21, 1998 filing date of the underlying Boyce et al.

application to the February 6, 1998 *effective* filing date of the application herein. The Examiner's previous assertion that a Rule 131 declaration must show that the claimed invention worked for its intended purpose does *not* apply in the case of a declaration relying upon a showing of *conception* of the claimed invention. A showing that a claimed invention worked for its intended purpose is only required in the case of an *actual reduction to practice*. See M.P.E.P. 715.07 (Three Ways to Show Prior Invention).

In view of the Boyce and Manrique declaration submitted herein, applicants respectfully submit that their declaration antedates, and therefore removes, the Boyce et al. '939 patent as a reference.

In the final Office Action, the Examiner rejected Claims 12 and 15-18 under 35 U.S.C. §103(a) for obviousness over Lyle. The Examiner asserts therein:

...Lyle discloses the use of a binding agent in general and of a crosslinking molecule of cyanoacrylate specifically but does not disclose the use of the particular crosslinking agents as claimed. However, the Examiner posits that it would have been obvious to use another crosslinking agent in view of the broad teaching of Lyle for a binding agent absent some showing that the particular agent had some unexpected/unobvious result.

As noted above in connection with the Examiner's rejection of the claims for alleged anticipation by Lyle, a cyanoacrylate adhesive works by becoming *mechanically* bound to the substrate. *There is no chemical bonding that takes place between cyanoacrylate and its substrate as evidenced by the two internet publications annexed hereto.*

It is well established that when obviousness is based on a particular prior art reference, there must be a showing of a suggestion or motivation to modify the teachings of that reference. *B.F. Goodrich Co. v. Aircraft Braking Systems Corp.*, (CAFC), 72 F.3d 1577, 1582, 37 USPQ2d 1314, 1318 citing *ACS Hosp. Sys., Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984). Lyle nowhere provides any suggestion, motivation or even a hint that the demineralized bone particles therein may be bonded to each other through chemical bonds formed between their collagen-exposed surfaces. Absent such a showing of a chemical linkage, Claims 12 and 15-18 are believed to be patentable over Lyle.

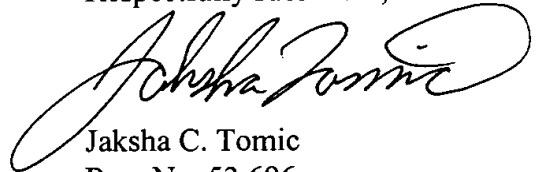
In the Office Action mailed September 25, 2001, the Examiner indicated that Claims 24-32, 46-54, 64-72 and 83-91 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The Examiner further indicated that Claims 33, 55, 73 and 92 would be allowable if rewritten to overcome the rejection under 35 U.S.C. § 112, second paragraph and to include all of the limitations of the base claim and any intervening claim.

By way of implementing the Examiner's proposals, applicants filed an Amendment on July 23, 2002 presenting new Claims 95-134 and cancelling Claims 8, 22, 44, 62 and 81 without prejudice. The Examiner declined to enter this Amendment on the unrelated ground that Claim 1, an independent claim, was amended to include a limitation that was only present in some dependent claims. On August 8, 2002, applicants filed a Request for Continued Examination which submitted the previous amendment filed July 23, 2002. The Examiner issued a non-final Office Action

rejecting pending Claims 1-7, 9-21, 23-43, 45-61, 63-80 and 82-134 based on the prior art of record. Since the Examiner rejected Claims 95-134 based on prior art of record after they had previously been indicated to be allowable over the prior art of record (if rewritten as suggested), applicants question whether the Examiner's subsequent rejection of these claims was made in error or whether the Examiner upon further reflection now regards these claims to be unpatentable over the prior art of record. The Examiner's clarification would be welcome on this point.

Further favorable consideration and allowance by the Examiner of pending Claims 1-7, 9-21, 23-43, 45-61, 63-80 and 82-144 are once again respectfully requested.

Respectfully submitted,



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